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Research Article

Cytotoxicity study of transdermal desloratadine delivery system on murine melanoma and human dermal fibroblast cell cultures

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Abstract

Introduction: Transdermal delivery of antihistamines is one of the ways to treat and prevent allergic conditions, reducing the adverse effects associated with oral administration.

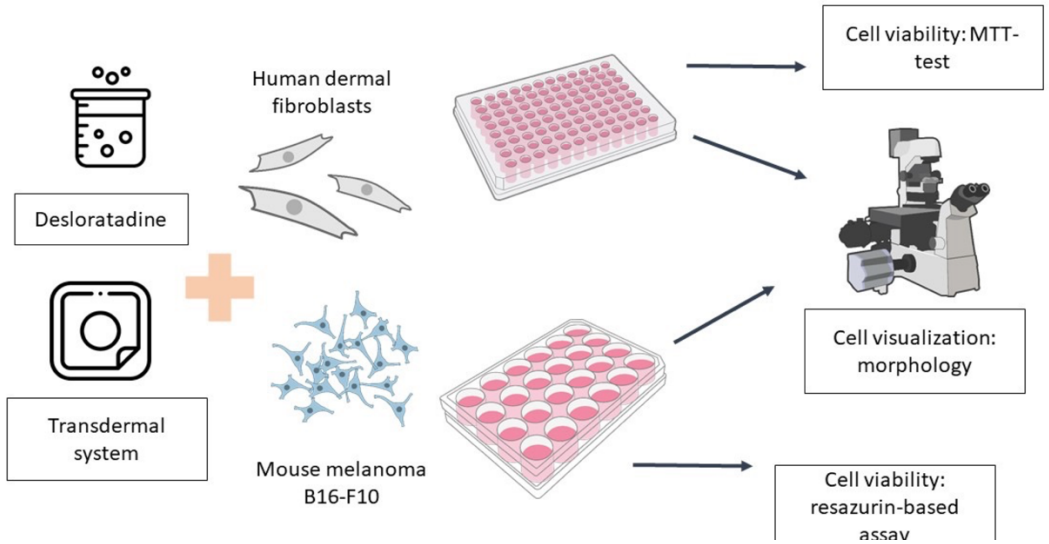
Materials and Methods: We evaluated the cytotoxicity of the transdermal desloratadine delivery system in micellar and ionic forms on murine melanoma and human dermal fibroblast cell cultures using the MTT assay and resazurin live cell assay.

Results: The results of the MTT assay demonstrated that desloratadine in micellar and ionic forms had a more pronounced cytotoxic effect on murine melanoma cells than on human dermal fibroblasts. The transdermal system had no effect on cell viability. Desloratadine in micellar or ionic form reduced cell viability: the survival rate of murine melanoma cells was below 50%, while when incubated with the transdermal system, the viability of human dermal fibroblasts was above 70%, indicating no toxicity.

Discussion: The polyvinylpyrrolidone-based transdermal system is not cytotoxic, but the active ingredient, desloratadine, features antiproliferative activity, to a greater extent, in relation to tumor cells.

Conclusion: The obtained results demonstrated the cytotoxic effect of micellar and ionic desloratadine on the tumor culture of murine melanoma and the biocompatibility of the transdermal desloratadine delivery system with human dermal fibroblasts.

Graphical abstract



Keywords

antihistamine, biocompatibility, human dermal fibroblasts, murine melanoma, patch, cytotoxicity

Introduction

Desloratadine (DL) is a non-sedating antihistamine approved for the treatment of allergic rhinitis or chronic idiopathic urticaria (Sadowska-Woda et al. 2010). Being a potent antagonist of human histamine H1 receptors, desloratadine features an anti-inflammatory activity in addition to the antihistamine one (Bousquet et al. 2004).

Desloratadine has a long-lasting effect and does not cause drowsiness, as it does not penetrate the central nervous system. DL is at least 50-fold more potent *in vitro* and appears to be 10-fold more potent *in vivo* than loratadine. The antihistamine is metabolized to 3-hydroxydesloratadine, which retains biological activity that is not mediated through the H1 receptor. This may be associated with inhibition of histamine-induced cytokines and proinflammatory mediators expression (Norman et al. 2001). Previous studies have suggested that desloratadine may have decongestant activity (Berger et al. 2002). As a result, this antihistamine is frequently used to treat a wide range of allergic conditions, as well as to prevent seasonal allergies.

The short half-life of antihistamines is one of their delivery problems, especially when the drug is administered through the gastrointestinal system. Therefore, transdermal delivery systems have become widespread, in which the active substance is accumulated in special patches, which, when applied to the skin, provide a long-term and uniform release of the active substance and its gradual absorption through the skin. The use of such transdermal systems requires initial evaluation of their biocompatibility and feasibility in living organisms. Biocompatibility of a substance is the ability to interact with cells and tissues without causing toxic or adverse effects. Studies to evaluate the biocompatibility of novel materials employ a variety of research methods, such as *in vitro* cell culture viability assessment, *in vivo* animal experiments, and clinical studies. The main methods used to assess the biocompatibility of transdermal drug delivery systems in cell cultures are the following: determining cell viability, studying changes in cell morphology, and monitoring mediator activity (Kawahara et al. 2007).

We have developed a transdermal way of delivery of desloratadine in ionic and micellar forms (Ageev et al. 2024). We also demonstrated the most optimal kinetics of desloratadine release from matrix patches carrying the antihistamine in its micellar form. The next stage of the study is to evaluate the cytotoxic effects and biocompatibility of the transdermal drug delivery system.

The purpose of this study was to test the cytotoxicity and biocompatibility of matrix patches in the form of a transdermal system containing desloratadine in micellar and ionic forms *in vitro*.

Materials and Methods

Study objects

We studied two types of previously developed matrix transdermal transport systems (TTS): the first contained desloratadine in ionic form (TTS-DI), and the second contained desloratadine incorporated into micelles (TTS-DM). The manufacturing technology of both TTS types is described in detail in our previous work (Ageev et al. 2024). The patches were made of a matrix containing the active ingredient and an adhesive base in the form of film Cruofilm, which was supposed to secure the patch to the skin. Polyvinylpyrrolidone K-30 was used as a matrix. In the case of TTS-DI, desloratadine was dissolved in the matrix; in the case of TTS-DM, it was added to it in the form of pre-prepared Tween-80-based micelles (Fluka, UK) with desloratadine dimethyl sulfoxide solution. Solutions of ionic desloratadine (DI), micellar desloratadine (DM), empty micelles and Cruofilm (China) film for cytotoxicity tests were pretreated at 110°C for 30 min; transdermal forms were pretreated at 110°C for 15 min.

Cell culture

The study was performed on a culture of murine melanoma cells (B16-F10), which is a mixture of fusiform and epithelium-like cells isolated from murine skin. Melanoma cells were cultured in a Thermo Scientific Midi40 incubator at 37°C and 5% CO_2 using DMEM medium (Paneco, Russia) supplemented with 10% fetal calf serum (INTL KANG, China) and 1% penicillin-streptomycin antibiotic solution (Servicebio, China) under normal conditions. When 80-90% confluency was reached, the cells were reseeded into culture plates for further cytotoxicity studies.

The cell line of immortalized human dermal fibroblasts (HDF) hTERT-HDFa (d220) was obtained from the Unique Scientific Facility "Cell Culture Collection" of the Institute of Developmental Biology of the Russian Academy of Sciences. The cells were cultured in a Thermo Scientific Midi40 incubator at 37°C and 5% CO_2 using DMEM medium (Paneco, Russia) supplemented with 10% fetal calf serum (INTL KANG, China) and 1% penicillin-streptomycin antibiotic solution (Servicebio, China) under normal conditions. When 80-90% confluency was reached, the cells were reseeded into culture plates for further cytotoxicity studies.

Cytotoxicity test

Cytotoxicity of individual components in the matrix patch (desloratadine in free and micellar forms), as well as a polymer, polyvinylpyrrolidone (PVP), was studied using the tetrazole dye 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-tetrazolium bromide (MTT). Viable cells form purple formazan crystals when incubated with yellow MTT. The cytotoxicity of the studied substances is assessed by the dissolved formazan optical density.

Desloratadine cytotoxicity was tested through seeding murine melanoma B16 cells in a 96-well plate at a concentration of 5 x 10^3 cells per well. The cells were treated with micellar desloratadine solution, empty micelles, and ionic desloratadine solution at concentrations ranging from 0.9 to 125 μg/mL. After 24 hours of incubation under standard conditions, the medium was replaced with serum-free medium spiked with 10 μl of MTT (5 mg/mL). After 3.5 hours, the formed formazan crystals were dissolved in 150 μl of DMSO. The absorbance was measured on a Varioscan Lux multimodal plate reader (Thermo Scientific, USA) at a wavelength of 570 nm versus 650 nm. The viability of melanoma was expressed as a percentage of control cells incubated in a complete nutrient medium.

Cytotoxicity on dermal fibroblast culture was studied in a 96-well plate at the cell concentration of 2.5 x10^3 per well. DI, DM, and empty micelles were added to the cells up to final concentration of 0.9–125 μg/mL and incubated under standard conditions. PVP was added up to final concentration of 0.2-85 mg/mL. After 24 hours, the MTT assay was performed. Fibroblast viability was expressed as a percentage of the control.

Cytotoxicity study of resazurin-based transdermal delivery system

The patch was tested in a 24-well plate. Murine melanoma cells (B16-F10) and HDF were seeded at a concentration of 2.5 x 10^4 per well. Then the transdermal system (TTS), TTS-DI (patch with desloratadine in ionic form) and TTS-DM (patch with desloratadine in micellar form) and Cruofilm were added to the cells. After 24 hours, cell viability was assessed by resazurin live cell assay. For this purpose, 50 μL of resazurin solution (Medchemexpress, USA) at the concentration of 0.15 mg/mL in a phosphate-buffered saline was added to 500 μL of medium in the wells, then incubated for 4 hours under standard conditions. After incubation, 200 μL of medium was transferred to a 96-well black plate. Fluorescence was measured using a Varioscan Lux multimodal plate reader (Thermo Scientific, USA) at Ex 560 and Em 590 nm. Viability was expressed as a percentage of control cells (complete nutrient medium).

Morphological evaluation of the cell culture

The morphology of murine melanoma cells and human dermal fibroblasts cultured with several TTS variants (TTS-DI, TTS-DM, and TTS), micellar, and ionic forms of desloratadine was examined using a Micromed I inverted microscope (Russia). Microscopic images were taken using a ToupTek microscope camera (China).

Statistics

Viability percentage calculation and statistical data processing were performed in Graphad Prizm 8. The data on murine melanoma cells MTT assay was processed using the Mann–Whitney U test; the data on resazurin live cell assay and the human dermal fibroblasts MTT assay were processed using one-way ANOVA with post hoc Tukey processing. The differences were considered as significant at $p<0.05$.

Results

A transdermal delivery system for the antihistamine drug desloratadine in ionic and micellar forms has been developed containing the polymer polyvinylpyrrolidone K-30. Figure 1 shows a photo of the patch.

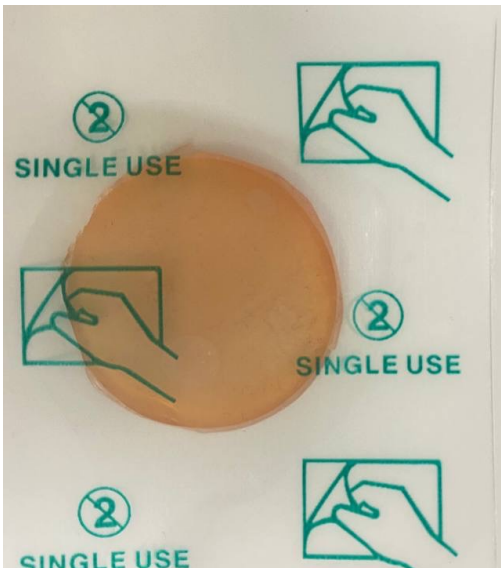


Figure 1. Photograph of the desloratadine transdermal delivery system.

One of the requirements for the properties of patches is biocompatibility. We then examined the impact of transdermal micellar and ionic desloratadine forms on cell culture viability. Additionally, we assessed the desloratadine active components (polymer and active substance) by colorimetric method to determine the transformation of yellow MTT salt to formazane crystals by viable cells with a high metabolic rate. Viability assessment was performed on two types of cell cultures – normal and tumor ones. Murine melanoma was used as the tumor cell line, and immortalized human dermal fibroblasts were used as the normal cells. We evaluated the main active ingredient of the transdermal form, desloratadine in ionic and micellar forms. Figure 2 shows data on the viability of B16-F10 cells after incubation with desloratadine in ionic (DI) and micellar (DM) forms, as well as with the micelles alone.

MTT assay showed that desloratadine in ionic form significantly inhibited the viability of murine melanoma cells at concentration of 15-125 μg/mL ($p<0.05$). The cell mortality rate was up to 95%. DI concentrations of 0.9-4 μg/mL did not result in substantial cell death. The micellar form of desloratadine showed a similar impact as the ionic form, with a statistically significant difference related to control cells ($p<0.05$). The melanoma survival rate was only 4-8%. At concentrations of 0.9-4 μg/mL, an impact on cell culture viability was also observed, with a cell survival rate of 66-77%. At these concentrations, the micellar form exhibited a reduced toxicity. Empty micelles in minor dilutions were cytotoxic for melanoma, with cell viability ranging from 8% at a 8-fold dilution (125 μg/mL of desloratadine) to more than 70% at over 128-fold dilutions (7.8 μg/mL of desloratadine). Morphological changes of melanoma cells incubated with ionic and micellar forms of desloratadine are shown in Figure 3.

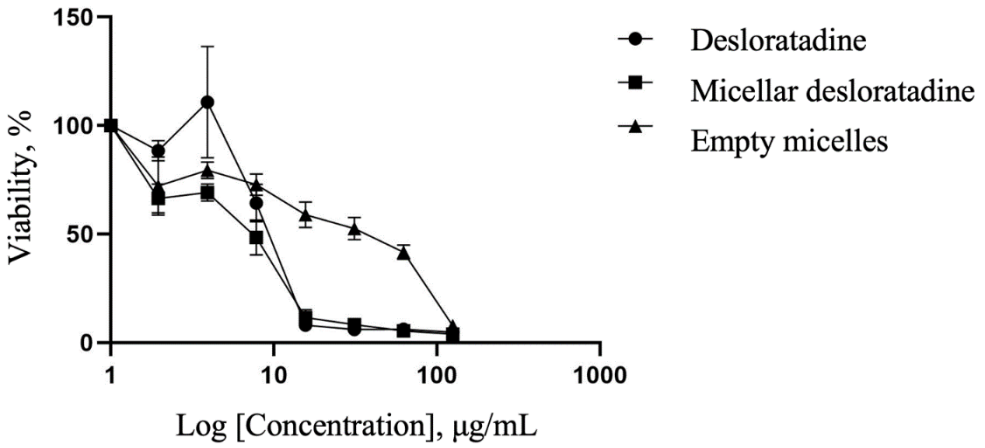


Figure 2. Results of cytotoxicity evaluation of desloratadine, micellar desloratadine and empty micelles (by desloratadine concentration) consisting of Tween-80 after 24 hours of incubation with murine melanoma B16-F10 cells.

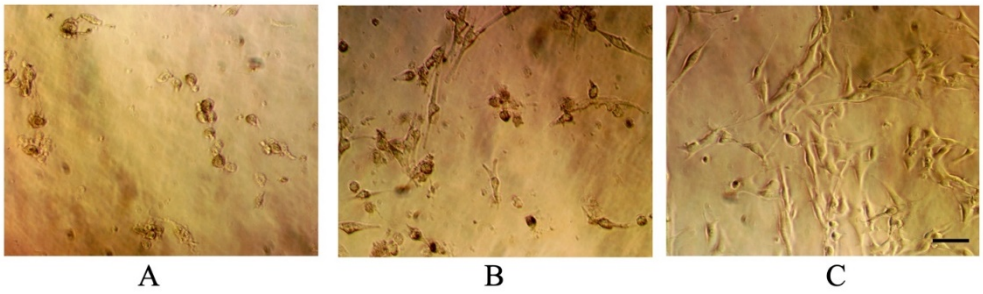


Figure 3. Microscopic images of the B16 melanoma cell line incubated for 24 hours with **A** – ionic desloratadine 15 μg/mL, **B** – micellar desloratadine 15 mg/mL, **C** – control cells. Scale bar – 50 μm.

Figure 3 shows that incubation of a murine melanoma cell line with ionic and micellar forms of desloratadine altered the cell morphology: the cells became rounder and their number reduced. Morphological changes are confirmed by the viability study data.

At the next stage, we analyzed the transdermal forms of ionic desloratadine (TTS-DI) and micellar desloratadine (TTS-DM). For this purpose, incubation was carried out in a 24-well plate. The cytotoxicity of Cruofilm and the transdermal system without desloratadine (TTS) was also investigated. The resazurin live cell assay (Fig. 4) showed that melanoma viability was 43% when incubated with TTS-DI and 33% when incubated with TTS-DM. The transdermal delivery system alone had no effect on the cell viability.

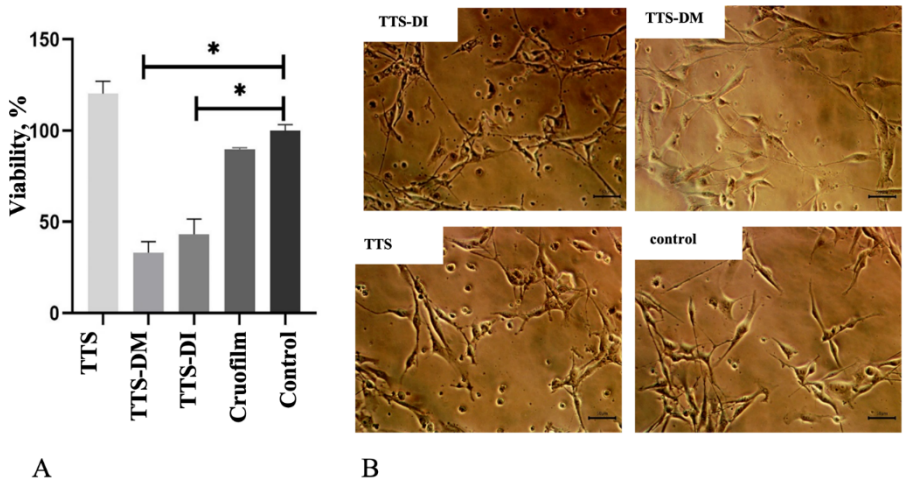


Figure 4. **A.** Viability of B16 murine melanoma cells after incubation with several TTS variants through the resazurin live cell assay. ***Note:*** * – $p<0.05$; **B** – microscopic images of cells after incubation with several TTS variants and control cells (10% DMEM), scale bar – 50 μm; TTS-DI – patch with desloratadine in ionic form; TTS-DM – patch with desloratadine in micellar form; TTS – transdermal system without desloratadine.

The primary constituents of the micellar and ionic desloratadine transdermal delivery method were also investigated on human dermal fibroblasts culture, involving an assessment of cell viability via the MTT assay and resazurin live cell assay. The results of the MTT assay on human dermal fibroblast (HDF) culture are shown in Figure 5.

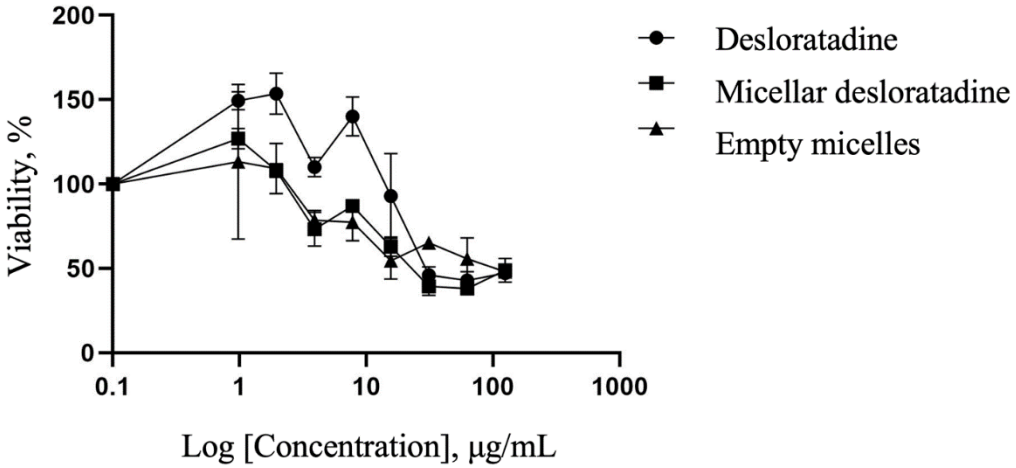


Figure 5. Cytotoxicity evaluation results of desloratadine, micellar desloratadine and empty micelles (by desloratadine concentration) after 24 hours of incubation with human dermal fibroblast cells.

MTT assay shows that desloratadine in micellar and ionic forms at concentrations of 31.5-125 µg/mL was cytotoxic for HDF; the cell viability was 39-57% ($p>0.05$). At concentrations below 31.5 µg/mL, desloratadine in ionic form was non-toxic. In micellar form, desloratadine had little or no effect on fibroblast viability at concentrations below 15 µg/mL. The viability when incubated with empty micelles at 8- and 16-fold dilutions was 48 and 49%, respectively. At higher dilutions, the viability of fibroblasts was more than 60%.

The cellular morphology of dermal fibroblasts was assessed after incubation with desloratadine in micellar and ionic forms (Fig. 6).

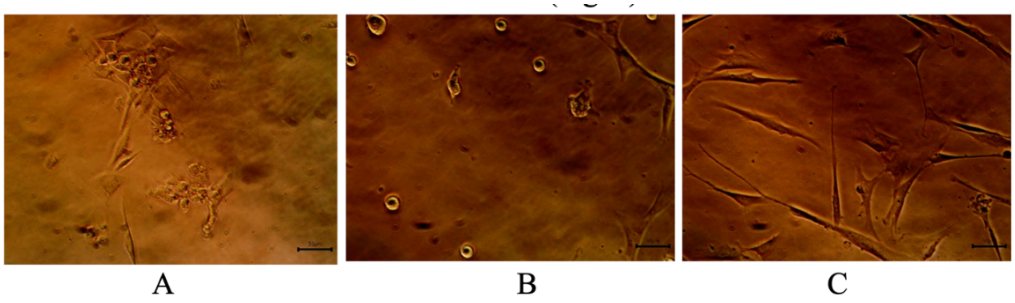


Figure 6. Microscopic images of human dermal fibroblast cell line incubated for 24 hours with **A** – ionic desloratadine 15 µg/mL, **B** – micellar desloratadine 15 mg/mL, **C** – control cells. Scale bar – 50 µm.

Morphological evaluation of HDF during incubation with desloratadine showed a greater number of rounded cells and fewer fusiform cells at concentrations of more than 15 µg/mL for micellar desloratadine and more than 31.25 µg/mL for the ionic form, in contrast to the control cells. At concentrations of 7.8 µg/mL and lower, cell morphology was identical to that of the control cells, which had not been exposed to any drugs.

Figure 7 shows an assessment of the HDF viability by resazurin live cell assay following incubation with TTS, TTS-DI and TTS-DM. As we can see from Figure 7, the viability of human dermal fibroblast cells during incubation with TTS after 24 hours under standard conditions was 83%, for TTS-DI and TTS-DM it was 71 and 73%, respectively. There is a slight inhibition of fibroblast viability when a transdermal delivery system with various forms of desloratadine is applied to them. Perhaps the toxic effects are related to desloratadine itself, which is part of the patch. The Cruofilm had little or no effect on fibroblast viability, as in the case of murine melanoma cells.

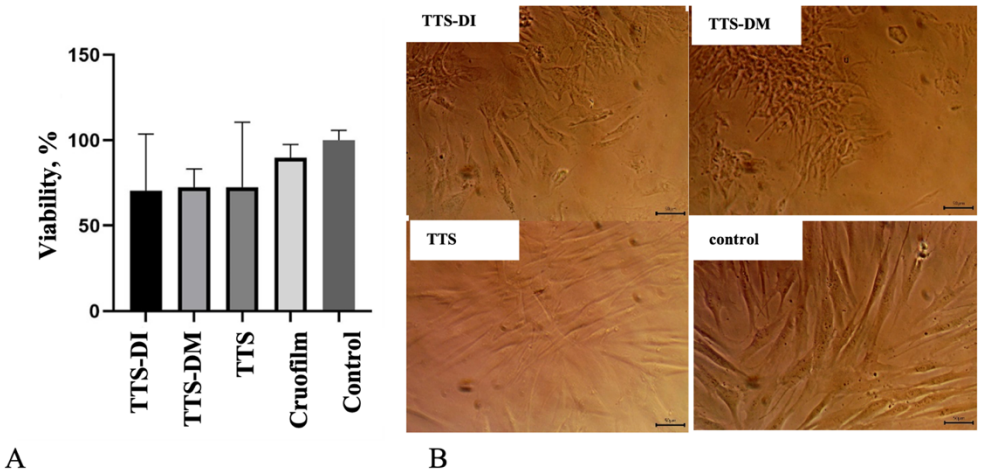


Figure 7. **A** – Viability of dermal fibroblasts after incubation with several TTS variants and Cruofilm through resazurin live cell assay, ***Note:*** * – p<0.05; **B** – microscopic images of cells after incubation with several TTS variants and control cells (10% DMEM), scale bar – 50 μm; TTS-DI – patch with desloratadine in ionic form; TTS-DM – patch with desloratadine in micellar form; TTS – transdermal system without desloratadine.

We analyzed the cytotoxicity of the polyvinylpyrrolidone polymer contained in the transdermal antihistamines delivery system. PVP was added to human dermal fibroblasts up to final concentrations of 0.2-85 mg/mL. The results are shown in Figure 8.

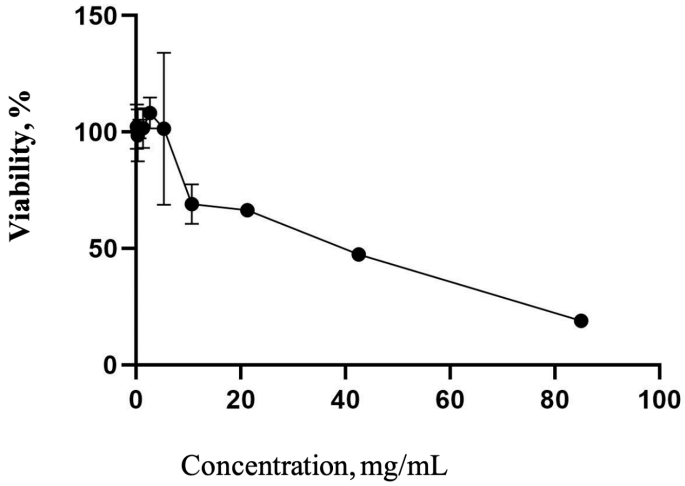


Figure 8. Cytotoxicity of polyvinylpyrrolidone by MTT assay with HDF after 24 hours of incubation.

The PVP polymer proved to be toxic to cells at only high concentrations of 21-85 mg/mL. Even at concentrations of less than 11 mg/mL, cytotoxicity was significantly reduced, and at 5 mg/mL, cell viability was 101%. The PVP IC_{50} was 33.72 mg/mL, which indicates a relatively low cytotoxicity of this polymer for human dermal fibroblasts.

We calculated the IC_{50} for the ionic and micellar forms of desloratadine for murine melanoma B16-F10 cells and human dermal fibroblasts (HDF). IC50 concentrations are shown in Table 1.

The results of the MTT assay demonstrated that desloratadine in micellar and ionic forms was more toxic to murine melanoma cells than to human dermal fibroblasts. It can be assumed that tumor cells are more sensitive to desloratadine. Transdermal systems alone showed as non-toxic in both murine melanoma cells and human dermal fibroblasts. The PVP polymer underlying the transdermal matrix is biocompatible with human dermal fibroblasts. The Cruophilm was non-cytotoxic to both cell cultures. The presence of desloratadine in micellar or ionic forms in the matrix patch affected the cell viability: murine melanoma cells survived at less than 50%, whereas human dermal fibroblasts survived at more than 70% when TTS-DM and TTS-DI were added. According to the standard ISO 10993-5 (2009), a material is considered non-toxic if the cell survival following contact is more than 70%. Thus, cytotoxicity experiments

have demonstrated that the transdermal system does not have a toxic effect on normal human dermal cells.

Table 1. IC50 of micellar and ionic desloratadine

Cell culture	IC_{50}, μg/mL	
	DI	DM
B16-F10	8.863	5.160
HDF	61.81	41.46

Note: HDF – human dermal fibroblasts; B16-F10 – culture of murine melanoma cells; DI – ionic desloratadine DM – micellar desloratadine.

The results of the MTT assay demonstrated that desloratadine in micellar and ionic forms was more toxic to murine melanoma cells than to human dermal fibroblasts. It can be assumed that tumor cells are more sensitive to desloratadine. Transdermal systems alone showed as non-toxic in both murine melanoma cells and human dermal fibroblasts. The PVP polymer underlying the transdermal matrix is biocompatible with human dermal fibroblasts. The Cruophilm was non-cytotoxic to both cell cultures. The presence of desloratadine in micellar or ionic forms in the matrix patch affected the cell viability: murine melanoma cells survived at less than 50%, whereas human dermal fibroblasts survived at more than 70% when TTS-DM and TTS-DI were added. According to the standard ISO 10993-5 (2009), a material is considered non-toxic if the cell survival following contact is more than 70%. Thus, cytotoxicity experiments have demonstrated that the transdermal system does not have a toxic effect on normal human dermal cells.

Discussion

The aim of this study was to assess the cytotoxic impact of a transdermal desloratadine delivery system in both ionic and micellar forms on murine melanoma cells and human dermal fibroblasts, which were used as models to test the effects of the matrix patch and its components on the skin tissue. The B16-F10 melanoma cell line is widely used to study cytotoxicity, as well as to study antitumor efficacy (Siwek et al. 2013)**.** Dermal fibroblasts are part of the human skin. This *in vitro* investigation assessed the cytotoxic effects of desloratadine in its ionic and micellar forms, as well as the transdermal delivery system, on murine melanoma cells, using an MTT assay as specified in ISO 10993-5 (2009). Viability assessment for the transdermal delivery system was performed through resazurin live cell assay. As noted by Lotfi et al. (2019), each cell has specific requirements for physical architecture and chemical composition, requiring a unique environment for optimal cellular function. Therefore, it is important to evaluate both the individual components and the entire transdermal drug delivery system.

The results of the MTT assay revealed the cytotoxic effect of both the ionic and micellar forms of desloratadine at concentrations greater than 15 μg/mL. Previous research revealed that desloratadine reduced the viability of human glioblastoma cell line U251 and primary culture of human glioblastoma cells (IC_{50} value 50 μM or 15 μg/mL) by elevating intracellular reactive oxygen species levels and caspase activity. Moreover, desloratadine decreased the expression of the major autophagy repressor mTOR and its upstream activator Akt and increased the expression of AMP-activated protein kinase (Vidicevic-Novakovic et al. 2022). In a study by Ma J. et al. (2020), suppression of bladder cancer cell viability (EJ and SW780 cell cultures) by desloratadine was demonstrated *in vitro*. Furthermore, desloratadine significantly reduced cell migration and invasion (Ma et al. 2020). In our study, desloratadine showed lower IC_{50} value for murine melanoma cells, specifically 8.863 μg/mL for ionic form and 5.160 μg/mL for micellar form, indicating some antitumor and antiproliferative activity. However, to confirm this, studies on laboratory animals are needed.

Literature data indicate that H1-type antihistamines suppress cytokine secretion by human and murine mast cells and basophils. Previous studies have shown that desloratadine significantly inhibited histamine release from human dermal mast cells. Preincubation with desloratadine significantly suppresses the expression of the mast cell activation marker, CD107a, as well as subsequent histamine release in primary human skin cells. Furthermore, the effect of desloratadine is not limited to IgE-dependent stimulation but also extends to IgE-independent pathways such as Ca-ionophore and substance P. Therefore, desloratadine can be considered as an effective mast cell stabilizer *in vitro*. Moreover, this effect is generally dose-dependent, with higher concentrations of desloratadine having a more powerful inhibitory effect. Desloratadine may exert an inhibitory effect on mast cells by interfering with either the accumulation of

intracellular calcium or the activation of intracellular calcium-dependent enzymes, such as calmodulin (Weller and Maurer 2009). The study by Lippert U. et al. (2000) showed that desloratadine also caused dose-dependent inhibition of TNF-alpha release from human leukemic mast cells (HMC-1) . Therefore, the transdermal form of desloratadine is quite effective in the treatment and prevention of allergic conditions, and our study showed an antiproliferative effect on murine melanoma cells and biocompatibility with human dermal fibroblasts.

Conclusion

The cytotoxicity of drugs and their delivery systems are studied for the initial assessment of the possibility of using the substance in humans. Transdermal drug delivery is marked by simplicity of administration and a decrease in the occurrence of adverse reactions associated with the active substance. It is important to evaluate this method of delivery for biocompatibility using various *in vitro* models with minimal use of laboratory animals. Our study assessed the biocompatibility of the transdermal desloratadine delivery system and its specific components, including active ingredients and the polymer polyvinypyrillidone. Thus, desloratadine *per se* has been used both in ionic and micellar forms. Both forms were toxic to murine melanoma cells at almost all concentrations studied, but were less toxic to human dermal fibroblasts. The PVP polymer exhibited low cytotoxicity *in vitro*. The transdermal delivery system based on this polymer had no significant effect on the either viability of murine melanoma or human dermal fibroblasts. The addition of desloratadine to the delivery system significantly reduced the viability of melanoma cells while having no effect on human fibroblasts.

Thus, cytotoxicity studies show that the transdermal antihistamine drug delivery system we have developed is biocompatible with human dermal fibroblasts with little effect on the viability of this cell culture.

Additional information

Conflict of interest

The authors declare the absence of a conflict of interests.

Funding

The authors have no funding to report.

Data availability

All of the data that support the findings of this study are available in the main text.

References

- Ageev AP, Zaborovskiy AV, Yunina DV, Tararina LA, Devkota MK, Andreev DN, Pyanzina AE, Shlyapkina VI, Buldygina YA, Kulikov OA, Pyataev NA (2024) Development of a transcutaneous form of desloratadine. Research Results in Pharmacology 10(2): 57–64. https://doi.org/10.18413/rrpharmacology.10.487
- Berger WE, Schenkel EJ, Mansfield LE, Desloratadine Study Group (2002) Safety and efficacy of desloratadine 5 mg in asthma patients with seasonal allergic rhinitis and nasal congestion. Annals of Allergy, Asthma, and Immunology 89(5): 485–491. https://doi.org/10.1016/S1081-1206(10)62086-8
- Bousquet J, Bindslev-Jensen C, Canonica GW, Fokkens W, Kim H, Kowalski M, Magnan A, Mullol J, van Cauwenberge P (2004) The ARIA/EAACI criteria for antihistamines: an assessment of the efficacy, safety and pharmacology of desloratadine. Allergy 59 (77): 4–16. https://doi.org/10.1111/j.1398-9995.2004.00577.x
- Danciu C, Falamas A, Dehelean C, Soica C, Radeke H, Barbu-Tudoran L, Bojin F, Pînzaru SC, Munteanu MF (2013) A characterization of four B16 murine melanoma cell sublines molecular fingerprint and proliferation behavior. Cancer Cell International 13: 75. https://doi.org/10.1186/1475-2867-13-75
- ISO 10993-5 (2009) Biological Evaluation of Medical Devices-Part 5: Tests for In Vitro Cytotoxicity. International Organization for Standardization: Geneve, Switzerland.
- Kazak M, Donmez N, Bahadori F, Yenigun VB, Kocyigit A (2020) A preliminary research study on the cytotoxicity of expired and non-expired composite resins: In vitro study. Odovtos 22(3): 227–238. https://doi.org/10.15517/ijds.2020.40455
- Lotfi A, Li H, Dao DV, Prusty G (2019) Natural fiber-reinforced composites: A review on material, manufacturing, and machinability. Journal of Thermoplastic Composite Materials 34(3): 089270571984454. https://doi.org/10.1177/0892705719844546
- Lippert U, Möller A, Welker P, Artuc M, Henz BM (2000) Inhibition of cytokine secretion from human leukemic mast cells and basophils by H1- and H2-receptor antagonists. Experimental Dermatology 9(2): 118–124. https://doi.org/10.1034/j.1600-0625.2000.009002118.x

- Ma J, Qi J, Li S, Zhang C, Wang H, Shao L, Yuan X, Sha Q (2020) Desloratadine, a novel antigrowth reagent for bladder cancer. Technology in Cancer Research & Treatment 19: 1533033820926591. https://doi.org/10.1177/1533033820926591
- Norman P, Dihlmann A, Rabasseda X (2001) Desloratadine: A preclinical and clinical overview. Drugs of Today 37(4): 215–227. https://doi.org/10.1358/dot.2001.37.4.620586
- Sadowska-Woda I, Sychta B, Rachel M, Bieszczad-Bedrejczuk E (2010) Protective effect of desloratadine against oxidative stress in human erythrocytes in vitro. Environmental Toxicology and Pharmacology 30(2): 141–146. https://doi.org/10.1016/j.etap.2010.05.001 [PubMed]
- Siwek B, De Pauw-Gillet MC, Quetin-Leclercq J, Angenot L, Bassleer R Characterization of non pigmented B16 melanoma cell-derived cytotoxic factors. Chemico-Biological Interactions 103(1): 59–73. https://doi.org/10.1016/s0009-2797(96)03752-0
- Kawahara K, Tojo K (2007) Skin Irritation in Transdermal Drug Delivery Systems: A Strategy for its Reduction. Pharmaceutical Research 24: 399–408. https://doi.org/10.1007/s11095-006-9165-4
- Vidicevic-Novakovic S, Stanojevic Z, Tomonjic N, Karapandza K, Zekovic J, Martinovic T, Grujicic D, Ilic R, Raicevic S, Tasic J, Isakovic A (2022) Proapoptotic and proautophagy effect of H1-receptor antagonist desloratadine in human glioblastoma cell lines. Medical Oncology 40(8): 241. https://doi.org/10.21203/rs.3.rs-1885564/v1
- Weller K, Maurer M (2009) Desloratadine inhibits human skin mast cell activation and histamine release. Journal of Investigative Dermatology 129(11): 2723–2726. https://doi.org/10.1038/jid.2009.134

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